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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 09/336,672 | 06/17/99 | HERRATH M | SCRIP1100 |

HM22/0112

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| EXAMINER | |
|---|---|
| SANDALS, W | |
| **ART UNIT** | **PAPER NUMBER** |
| 1636 | 14 |

**DATE MAILED:** 01/12/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Advisory Action

| Application No. | Applicant(s) |
|---|---|
| 09/336,672 | Von Herrath |
| **Examiner** | **Group Art Unit** |
| WILLIAM SANDALS | 1636 |

THE PERIOD FOR RESPONSE: [check only a) or b)]

a) ☐ expires _____ months from the mailing date of the final rejection.

b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☒ Appellant's Brief is due two months from the date of the Notice of Appeal filed on *Dec 28, 2000* (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

**Applicant's response to the final rejection, filed on *Dec 28, 2000* has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:**

☒ The proposed amendment(s):

☒ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

☐ will not be entered because:

☐ they raise new issues that would require further consideration and/or search. (See note below).

☐ they raise the issue of new matter. (See note below).

☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

☒ Applicant's response has overcome the following rejection(s):
*The rejection of the claims under 35 USC 102.*

☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☒ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:
*See Attached*

☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: _____

Claims objected to: _____

Claims rejected: 1-~~38~~ 36

☐ The proposed drawing correction filed on _____ ☐has ☐has not been approved by the Examiner.

☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ .

☒ Other *See Attached.*

***Response to Amendment***

1. The declaration under 37 CFR 1.132 filed December 28, 2000, Paper No. 13, is insufficient to overcome the rejection of claims 1-36 based upon 35 USC 112, first paragraph, scope of enablement, as set forth in the last Office action because:

The declaration presents evidence based upon the mouse model system, which is already indicated as enabled, but does not address the rejection based upon the lack of a nexus between the mouse model system and the broad basis of the claimed invention; Treatment of type I diabetes.

2. In addition, the data presented in the Declaration, Paper No. 13, have several problems:

a) the abscissa in the graph of Figure 1 in Paper No. 13 is labelled as "% Diabetes", but the legend and body of the text appear to indicate that the data represented is percentage of mice with diabetes. The body of the text also indicates that a measurement may be made as to a percentage or degree of progression of the disease in individual mice, and this raises doubt as to the actual meaning of the label "%Diabetes".

b) the data presented in Figure 2 of Paper No. 13 do not explain why the controls for GAD are not equal to the controls for InsB. They appear to be the same cells, and therefore should give the same responses, yet the data show the controls of GAD and InsB as being markedly different.

c) the data in Table 2 of Paper No. 13 shows that ***only*** IL-4 provided any benefit in the claimed method. The other cytokines tested either showed no clear effect or they had a negative effect, and would not be desirable in the method. Specifically, the data showed that an increase in INF-gamma was associated with onset of type-I diabetes. Therefore, increasing the levels of INF-gamma would have a undesirable effect on the claimed method of treatment, which is in contradiction to the method as claimed in claims 8, 19 and 29.

***Response to Arguments***

3. Arguments set forth in Paper No. 12, filed December 28, 2000 assert that the prior art as taught by Giannoukakis et al. was only pertinent to methods of treatment of type-I diabetes by introduction of islet cells. This is not the case, and at pages 2107 to 2114, the body of the discussion and Figures presents detailed description of proposed treatments for type-I diabetes by direct introduction of genes into the host recipients (see especially the bottom of column 2, page 2112 bridging to the top of column 1, page 2113, and Figure 2).

4. Arguments set forth in Paper No. 12 assert that the prior art as taught by Giannoukakis et al. did not address the treatment of an individual with a DNA encoding a gene. Giannoukakis et al. did in fact discuss just a few of the many problems associated with gene therapy at pages 2108 to 2109, where they point out the limitations of a few of the vectors currently being employed in gene therapy experimentation. The key point which is relevant to the instant claimed invention, however, is that no showing of any success in treatment of diabetes type-I by injection of DNA

encoding a gene has been demonstrated, despite the many attempts to introduce DNA vectors for treatments, including those which are referred to by Giannoukakis et al.

5. Arguments set forth in Paper No. 12, page 11, assert that insulin and GAD are known self-antigens, and that treatment and prevention of autoimmune diabetes would follow from the induction of type-II immunity to GAD and insulin. Then at page 16, bottom, bridging to the top of page 17 it is asserted that production of an anti-GAD antibody did not produce an inhibitory response for a method of treatment in the prior art as taught by Liu et al. These arguments are contradictory. The response to the first argument: that insulin and GAD are known self-antigens, and that treatment and prevention of autoimmune diabetes would follow from the induction of type-II immunity to GAD and insulin, is an argument contradicted at pages 16-17 as noted above. In respect to the rejection of the instant claimed invention over scope of enablement; the production of an antibody response to GAD or insulin, would not per se, lead to the clear knowledge that a treatment had been effected, and therefore would not be sufficient to instruct one of skill in the art as to the likelihood of success of a method of treatment emanating from the induction of an anti-GAD or anti-insulin antibody. (which is to say that I agree with the argument presented at pages 16-17 against the notion that the mere production of an antibody response as taught by Liu et al. is sufficient guidance to lead one of skill in the art to the conclusion that this constitutes a method of treatment.) Therefore, the assertion that the induction of an immune response to insulin or GAD would lead one to a conclusion that

treatment has been effected is not a true statement, and the argument is therefore not found convincing, and the rejection stands.

6. Arguments set forth in Paper No. 12 assert that the term "biological response modifier" is defined in the specification at pages 26 and 27. The definition in the specification merely states that among other things, a biological response modifier may include such things as a cytokine. This is not a definition, and does not provide one of skill in the art with a clear understanding of what is meant by the term "biological response modifier". The provision of a definition of the term by another document does not cure the deficiency, since the instant specification is not consistent with the definition of the referenced document.

7. The argument set forth in Paper No. 12 regarding the lack of antecedent basis for the phrase "nucleic acid construct" has not been found convincing. Insertion of the word "the" before the phrase would cure the defect.

8. The argument set forth in Paper No. 12 regarding the meaning of the phrase "non-pathogenic...Th lymphocytes" has not been found persuasive. The terms used to provide a basis for definition presented in Paper No. 12 are not found in the specification, and therefore, the phrase does not have a clear and unambiguous meaning. The assertion that "a T helper cell which does not contribute to the production of an autoimmune disease" is a definition for a non-pathogenic T helper cell does not provide a well established meaning in the prior art. The recited definition provided from Webster's II New College Dictionary of the meaning of the word "pathogenic" does not provide a definition for the word "non-pathogenic".

9. Arguments regarding the rejection of the claims under 35 USC 102 have been found convincing and the rejections are withdrawn.

***Conclusion***

10. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Friday from 8:30 AM to 5:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richard Schwartz can be reached at (703) 308-1133.

Any inquiry of a general nature or relating to the status of this application should be directed to the Zeta Adams, whose telephone number is (703) 305-3291.

William Sandals, Ph.D.
Examiner
January 8, 2001

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER